Regular Scaffolds for Bone Tissue Engineering: Geometry Optimization with a Mechanoregulation Algorithm

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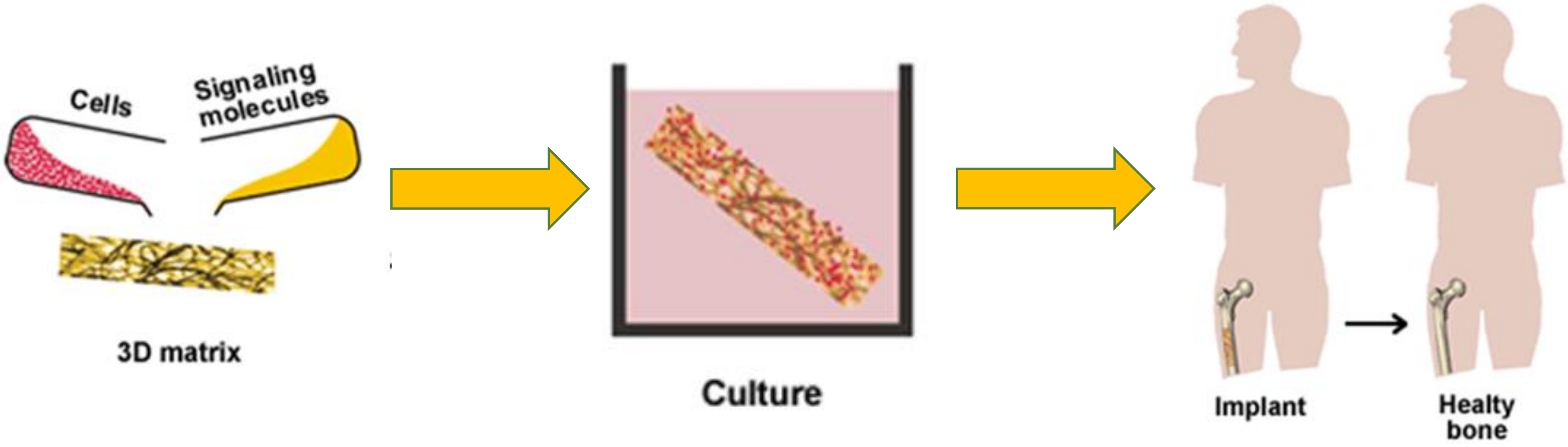
Motivation

Bone defects of critical dimensions, whether induced by primary tumour resection, trauma or selective surgery, present usually harsher challenges to the successful treatment for bone tissue repair. In such a case, the implantation of a scaffold is required in order to provide an ad-hoc structural/porous framework for the bone defect healing process.



The geometry of porous scaffolds has recently been shown to significantly influence the cellular response and the rate of bone tissue regeneration.

Zadpoor AA. Bone tissue regeneration: the role of scaffold geometry. Biomater Sci. 2015; 3: 231-45

Motivation

The development of the recent additive manufacturing techniques and, consequently, the possibility of building constructs with very sophisticated geometries, led many researchers to investigate the scaffold geometries that mostly favor the formation of bone in the shortest time. To this purpose, both regular and irregular scaffold geometries were proposed and investigated.

Motivation

- Identifying certain geometrical features that could potentially affect bone tissue regeneration requires studying different classes of pore shapes in a systematic way. Using a certain class of pore shape allows for isolating the effects of different geometrical features from each other and identifying new geometrical features that could potentially be useful for stimulating and guiding the process of bone tissue regeneration. No such studies are currently available in the literature.
- The most common approaches utilized in bone tissue engineering require costly protocols and time-consuming experiments.
- Computational models allow to simulate within a certain degree of accuracy how environment affects bone regeneration and hence, to fully understand the mechanisms behind tissue differentiation.

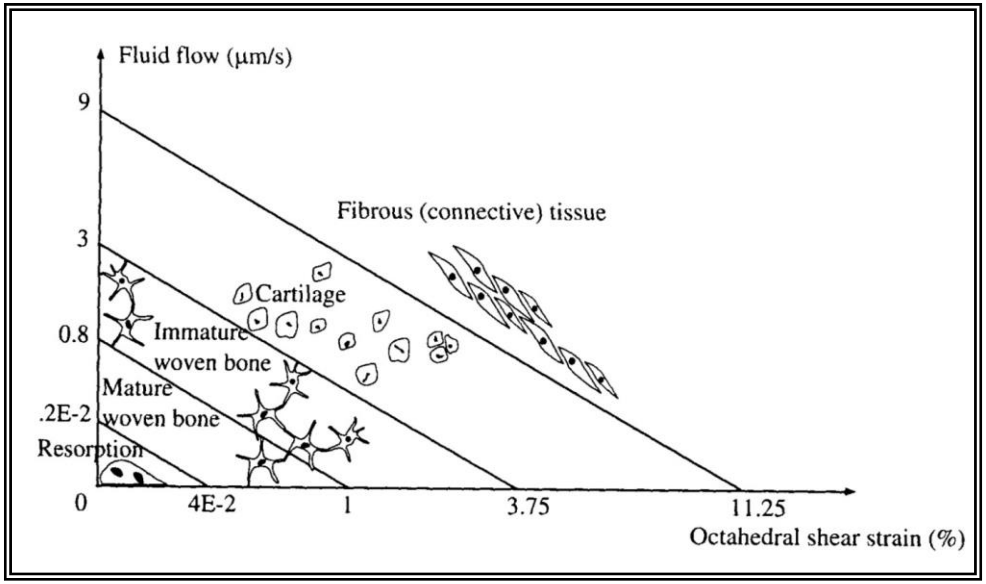
Zadpoor AA. Bone tissue regeneration: the role of scaffold geometry. Biomater Sci. 2015; 3: 231-45

The computational approach based on the mechanobiological model of Prendergast-Huiskes

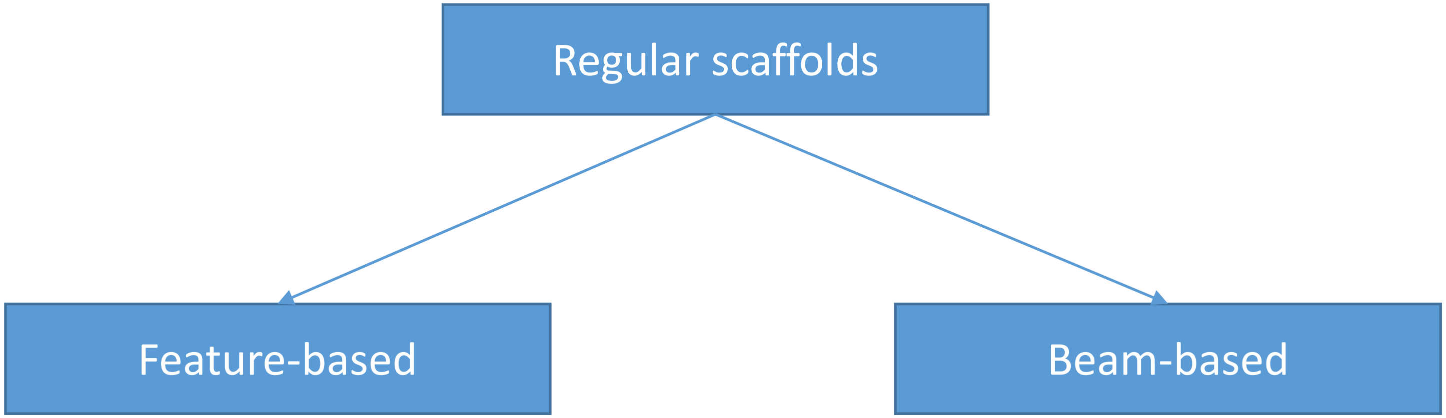
The fracture domain can be described as a biphasic poroelastic material. The biophysical stimulus that regulates the differentiation process of the mesenchymal stem cells is hypothesized to be a function of the octhaedral shear strain γ and of the interstitial fluid flow ν

$$S = \frac{\gamma}{a} + \frac{v}{b} \qquad (1)$$

$$IF \begin{cases} S > m \Rightarrow fibroblasts: \quad connective \ \ fribrous \ tissue \\ 1 < S < m \Rightarrow chondrocites: \ \ cartilage \\ n_{mature} < S < 1 \Rightarrow osteoblasts: \ \ immature \quad bone \\ n_{resorbtion} < S < n_{mature} \Rightarrow osteoblasts: \quad mature \quad bone \\ 0 < S < n_{resorbtion} \Rightarrow osteoclasts: \quad bone \quad resorption \end{cases} \qquad (2)$$



Classification



Regular scaffolds

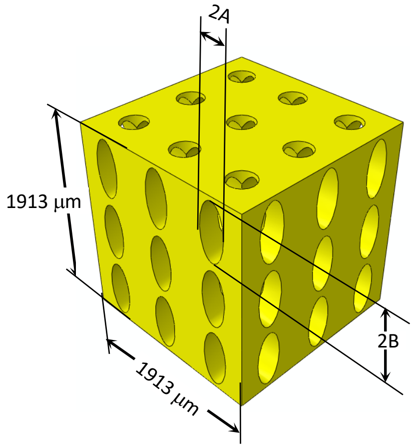
Feature-based

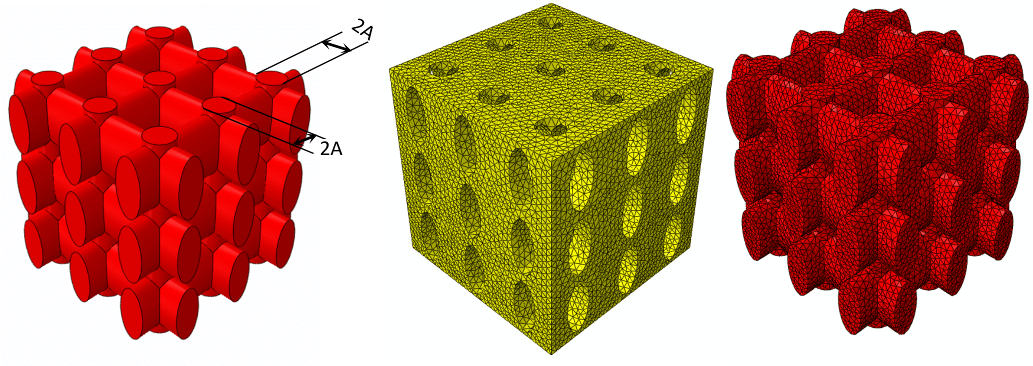
Beam-based

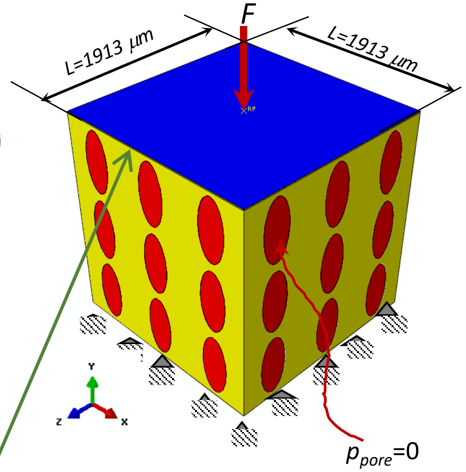
Regular Feature-based Scaffolds

Hexahedral unit cell with elliptical or rectangular pores

geometry (i): aligned elliptic pores, 3 × 3 pore/face



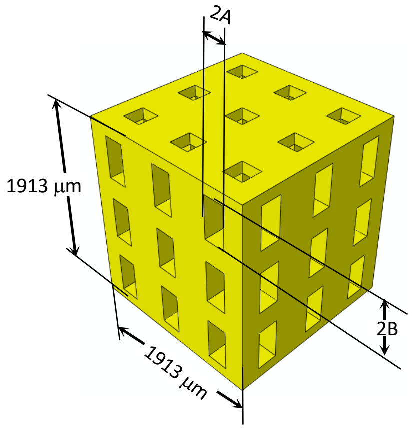


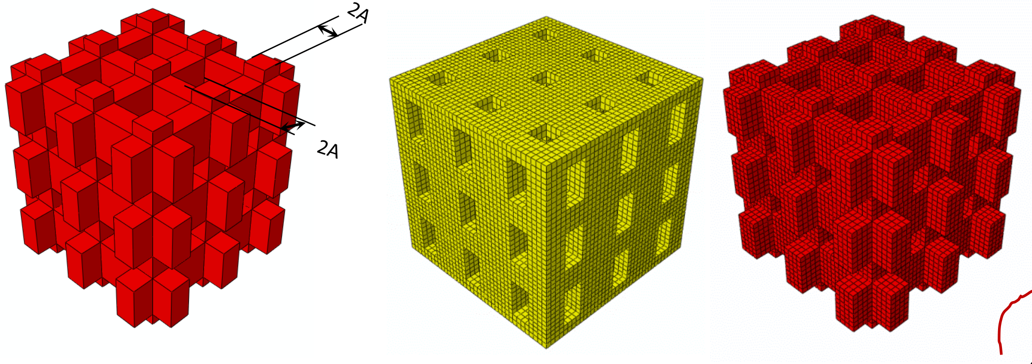


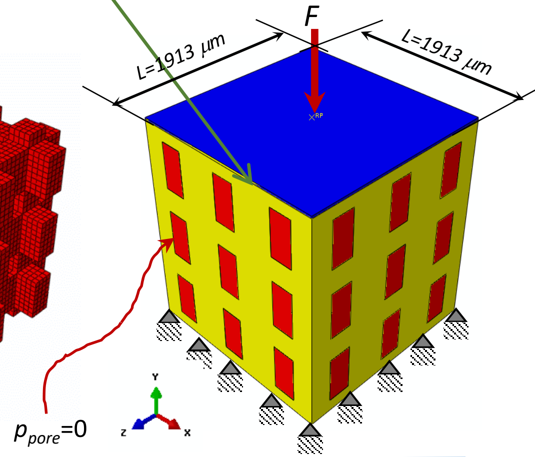
Constraint equations have been used between the plate and the upper surface of the model so as to have:

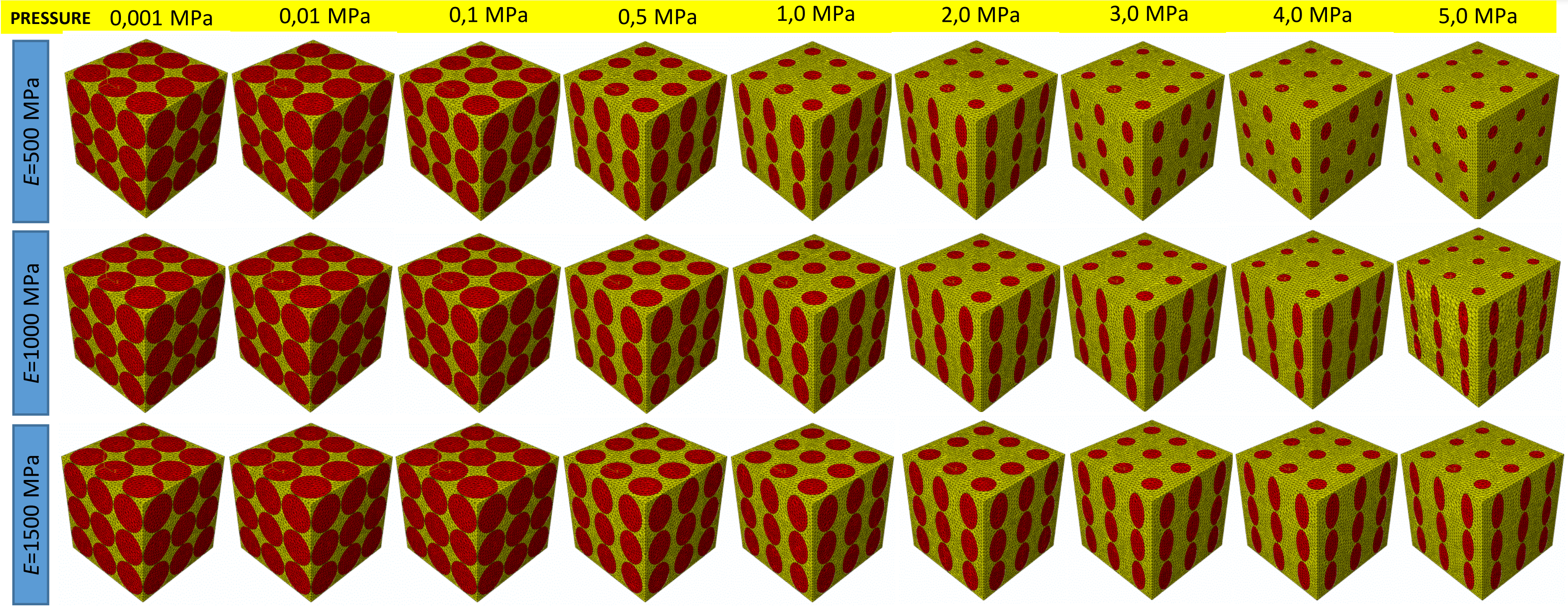
$u_{y(scaffold)}=u_{y(granulation\_tissue)}$

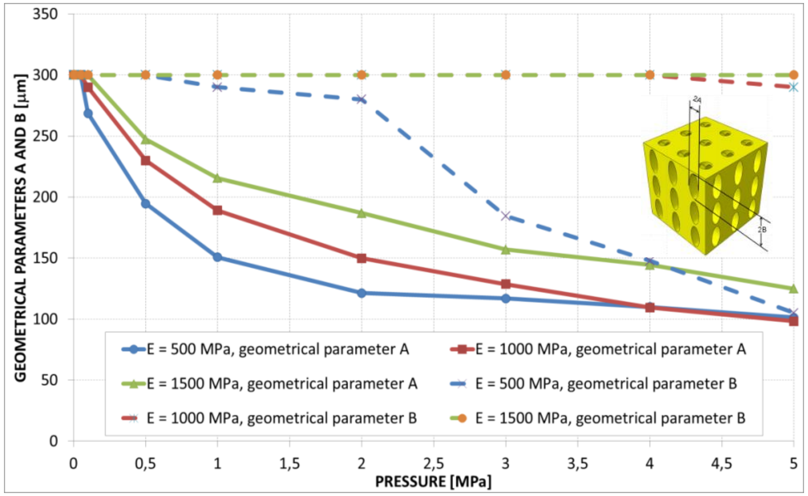
geometry (iii): aligned rectangular pores, 3 × 3 pore/face





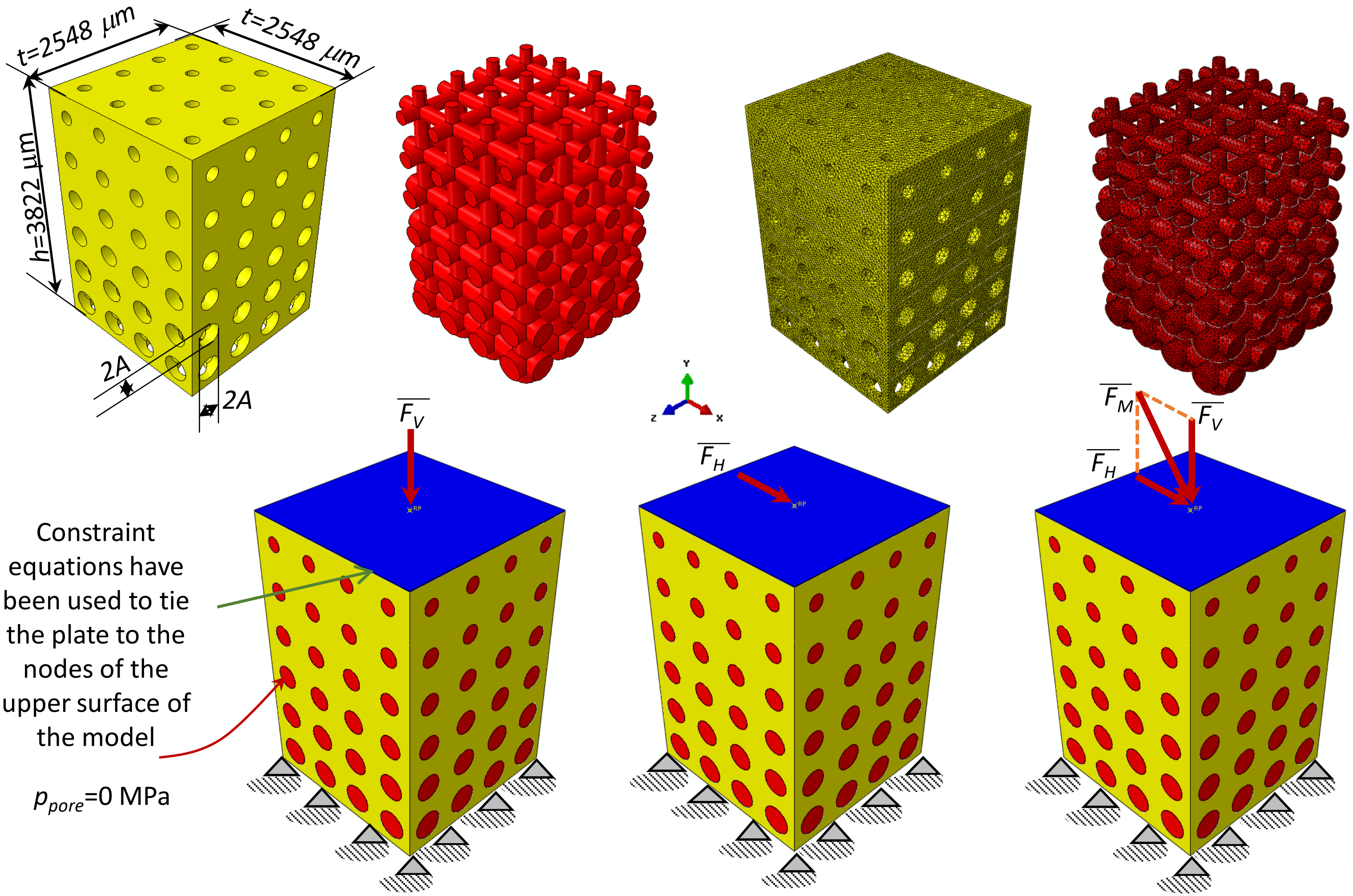






A. Boccaccio, A.E. Uva, M. Fiorentino, L. Lamberti, G. Monno, 2016. *A Mechanobiology-based Algorithm to Optimize the Microstructure Geometry of Bone Tissue Scaffolds.* International Journal of Biological Sciences, **12**, 1-17

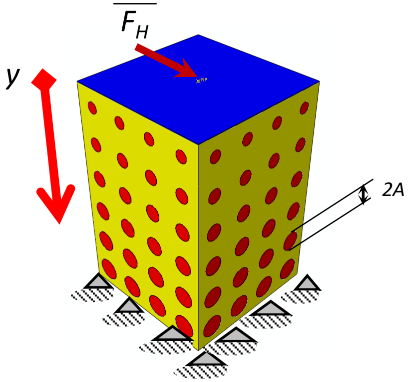
Hexahedral unit cell with circular pores: functionally graded porosity

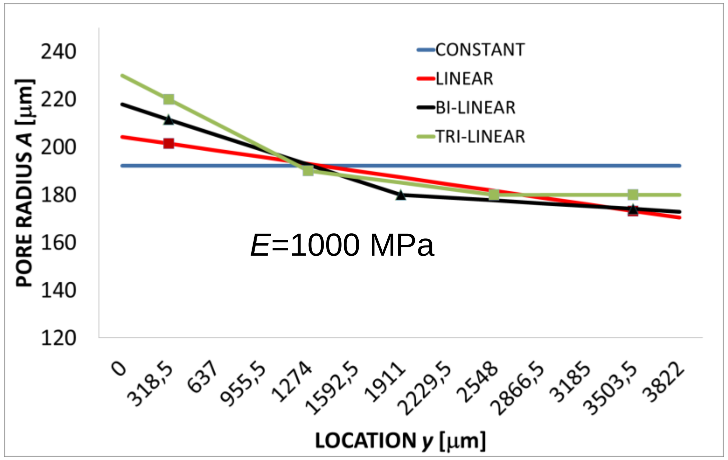


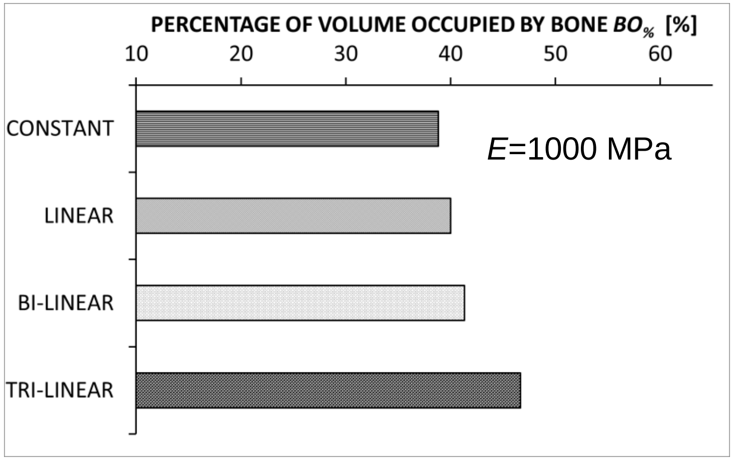
Constraint equations have been used to tie the plate to the nodes of the upper surface of the model

p_{pore}=0 MPa

Hexahedral unit cell with circular pores: functionally graded porosity

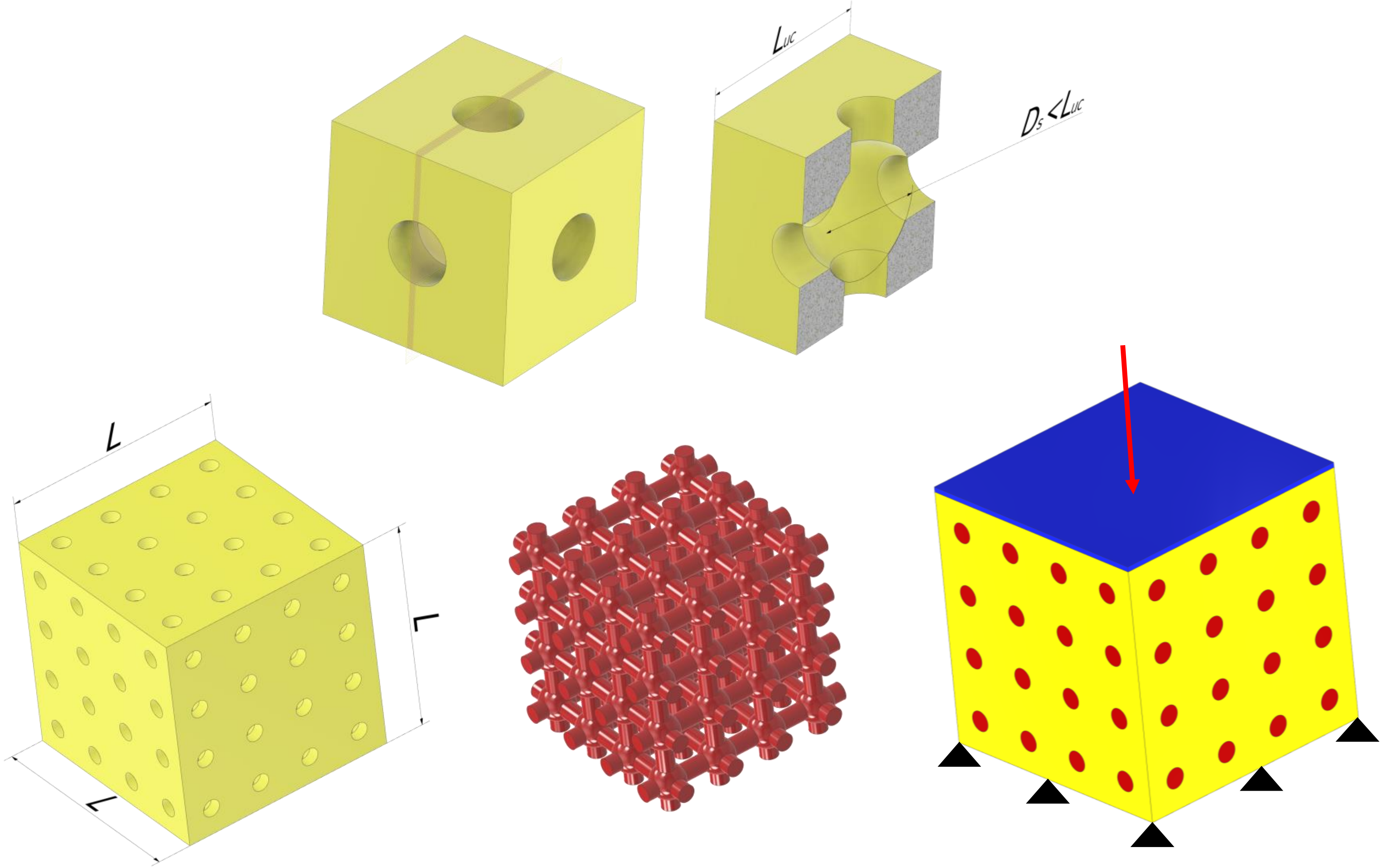




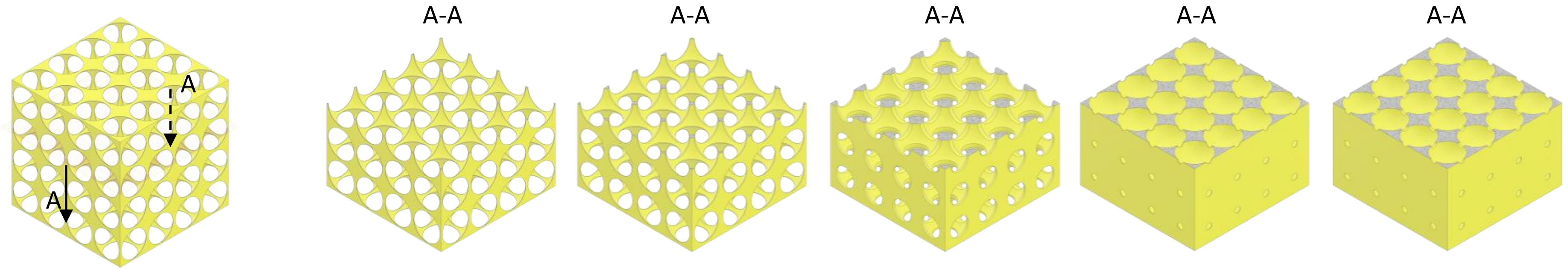


A. Boccaccio, A.E. Uva, M. Fiorentino, G. Mori, G. Monno, 2016. Geometry Design Optimization of Functionally Graded Scaffolds for Bone Tissue Engineering: A Mechanobiological Approach. PLoS ONE, 11: e0146935 (i.f. 3.234 Web of Science 2014).

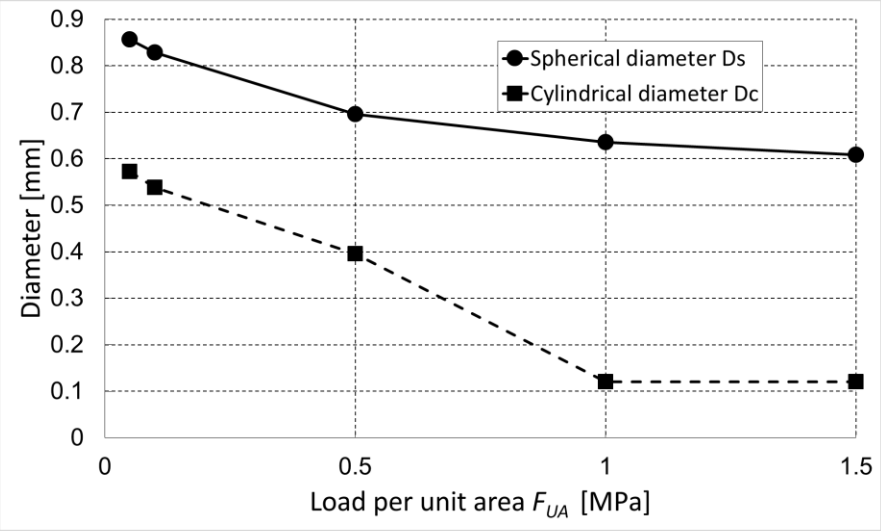
Spherical pores with cylindrical interconnections



Spherical pores with cylindrical interconnections



F_{UA} = 0.05 MPa F_{UA} = 0.10 MPa F_{UA} = 0.50 MPa F_{UA} = 1.00 MPa F_{UA} = 1.50 MPa

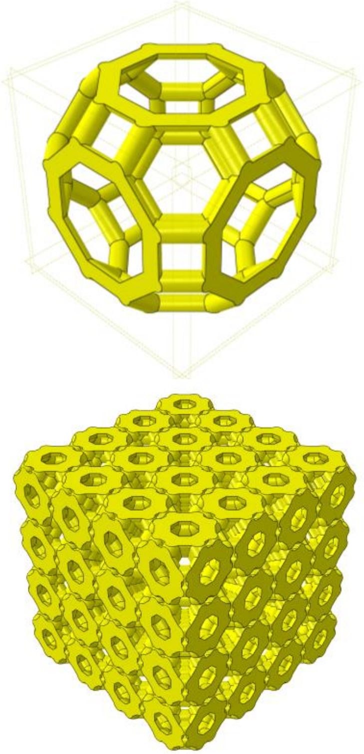


Óscar Libardo Rodríguez-Montaño, Carlos Julio Cortés-Rodríguez, Antonio Emmanuele Uva, Michele Fiorentino, Michele Gattullo, Vito Modesto Manghisi, Antonio Boccaccio (2020). An algorithm to optimize the micro-geometrical dimensions of scaffolds with spherical pores. Materials, vol. 13, 4062, ISSN: 1996-1944, doi: 10.3390/ma13184062

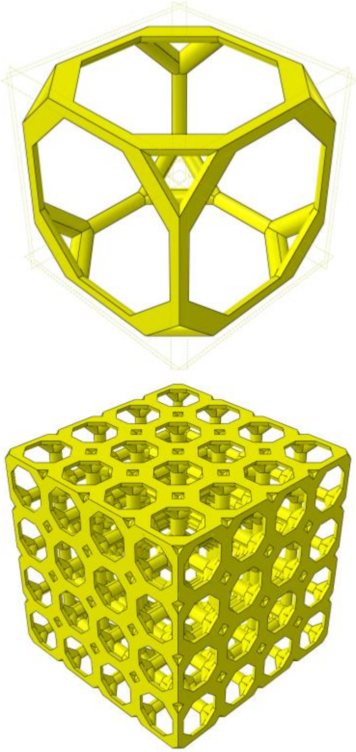
Regular Beam-based Scaffolds

Regular Beam-based Scaffolds

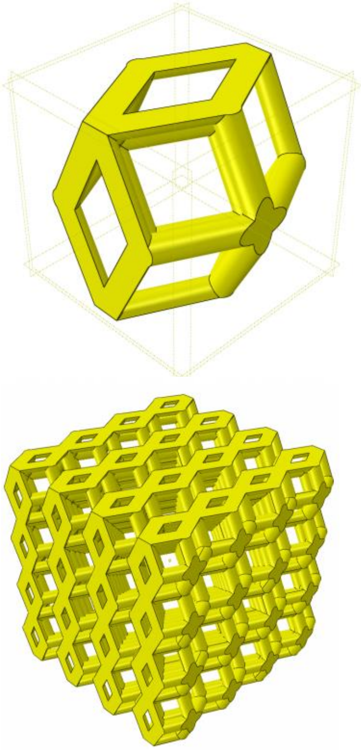
Truncated cuboctahedron



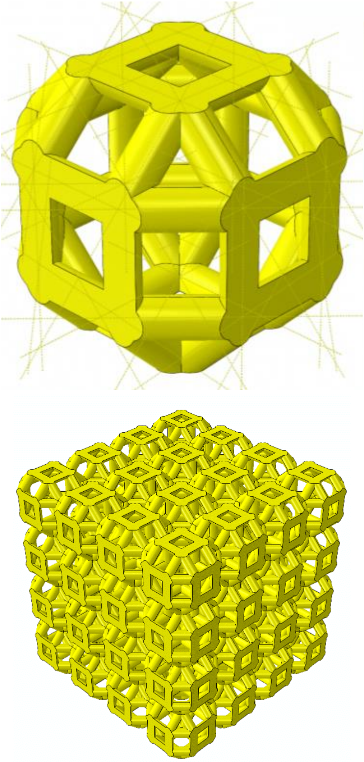
Truncated cube



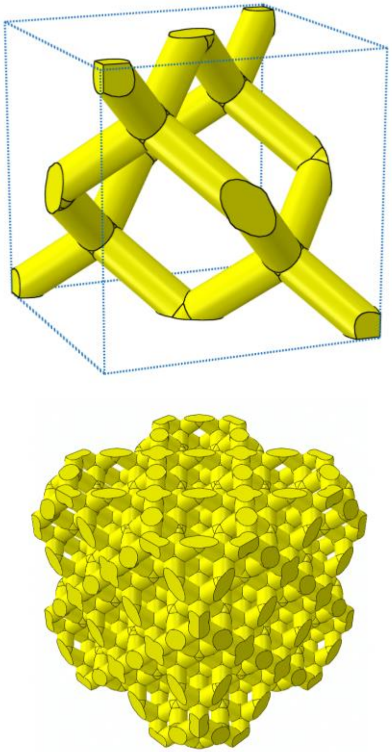
Rhombic dodecahedron



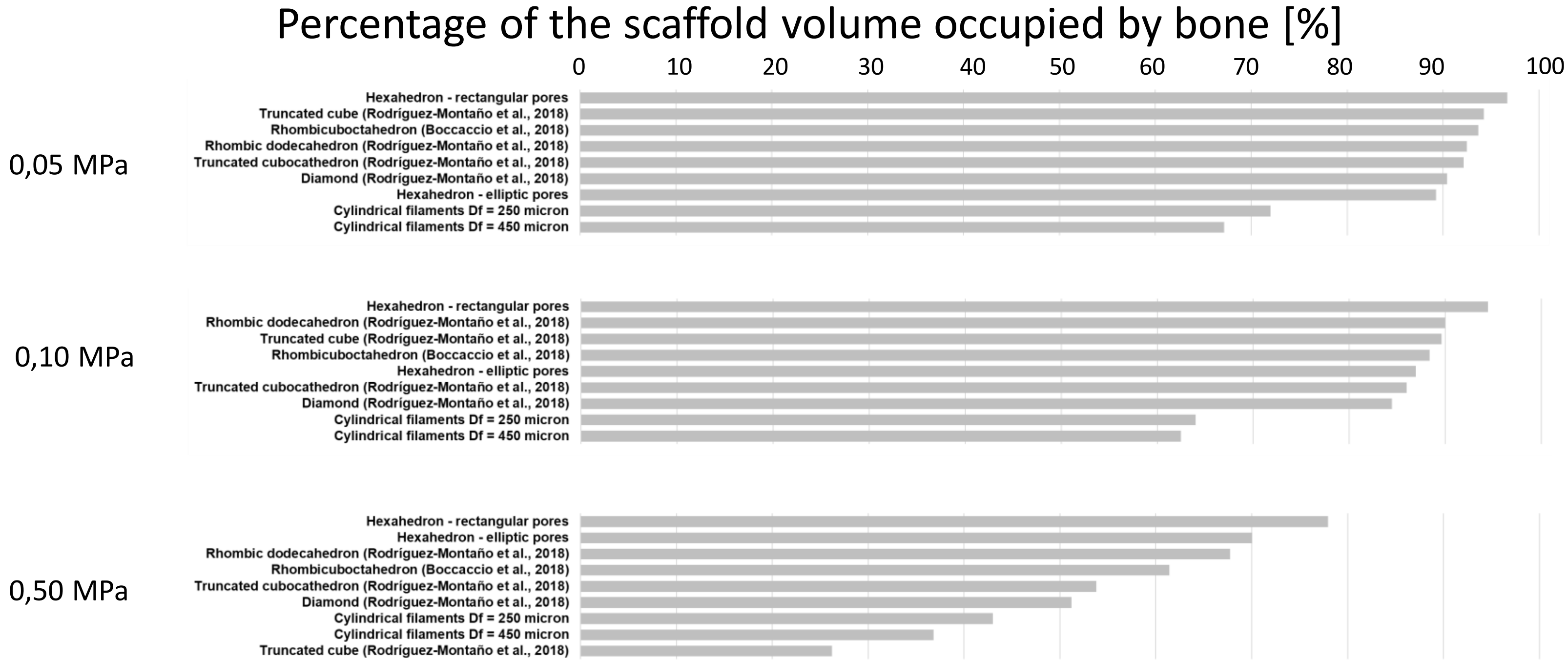
Rhombicuboctahedron

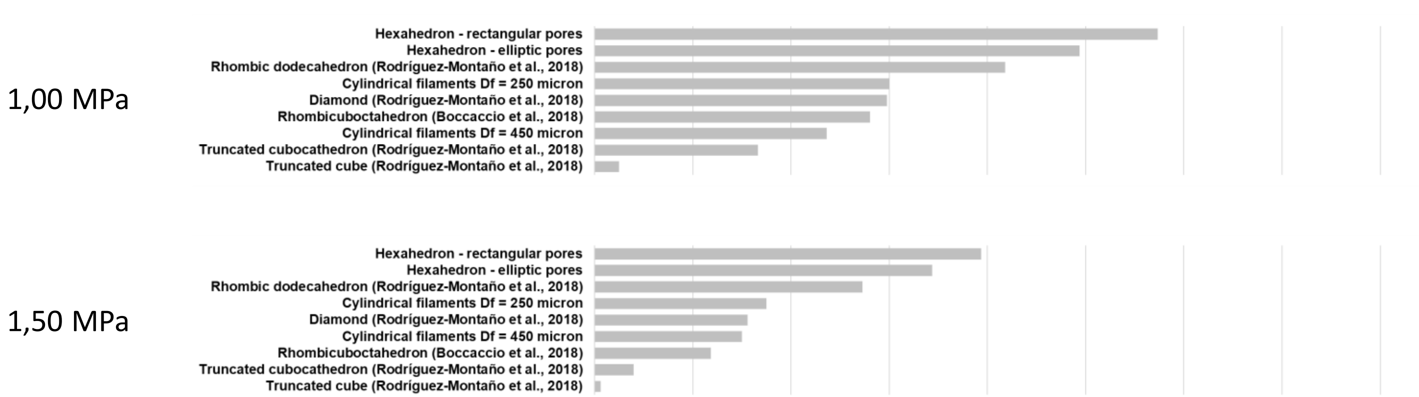


Diamond



Comparison


Percentage of the scaffold volume occupied by bone [%]
0
10
20
30
40
50
60
70
80
90
100
0,05 MPa
Hexahedron - rectangular pores
Truncated cube (Rodríguez-Montaño et al., 2018)
Rhombicuboctahedron (Boccaccio et al., 2018)
Rhombic dodecahedron (Rodríguez-Montaño et al., 2018)
Truncated cubocathedron (Rodríguez-Montaño et al., 2018)
Diamond (Rodríguez-Montaño et al., 2018)
Hexahedron - elliptic pores
Cylindrical filaments Df = 250 micron
Cylindrical filaments Df = 450 micron
0,10 MPa
Hexahedron - rectangular pores
Rhombic dodecahedron (Rodríguez-Montaño et al., 2018)
Truncated cube (Rodríguez-Montaño et al., 2018)
Rhombicuboctahedron (Boccaccio et al., 2018)
Hexahedron - elliptic pores
Truncated cubocathedron (Rodríguez-Montaño et al., 2018)
Diamond (Rodríguez-Montaño et al., 2018)
Cylindrical filaments Df = 250 micron
Cylindrical filaments Df = 450 micron
0,50 MPa
Hexahedron - rectangular pores
Hexahedron - elliptic pores
Rhombic dodecahedron (Rodríguez-Montaño et al., 2018)
Rhombicuboctahedron (Boccaccio et al., 2018)
Truncated cubocathedron (Rodríguez-Montaño et al., 2018)
Diamond (Rodríguez-Montaño et al., 2018)
Cylindrical filaments Df = 250 micron
Cylindrical filaments Df = 450 micron
Truncated cube (Rodríguez-Montaño et al., 2018)


1,00 MPa
Hexahedron - rectangular pores
Hexahedron - elliptic pores
Rhombic dodecahedron (Rodríguez-Montaño et al., 2018)
Cylindrical filaments Df = 250 micron
Diamond (Rodríguez-Montaño et al., 2018)
Rhombicuboctahedron (Boccaccio et al., 2018)
Cylindrical filaments Df = 450 micron
Truncated cubocathedron (Rodríguez-Montaño et al., 2018)
Truncated cube (Rodríguez-Montaño et al., 2018)
1,50 MPa
Hexahedron - rectangular pores
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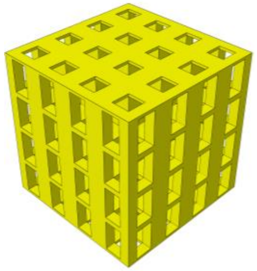
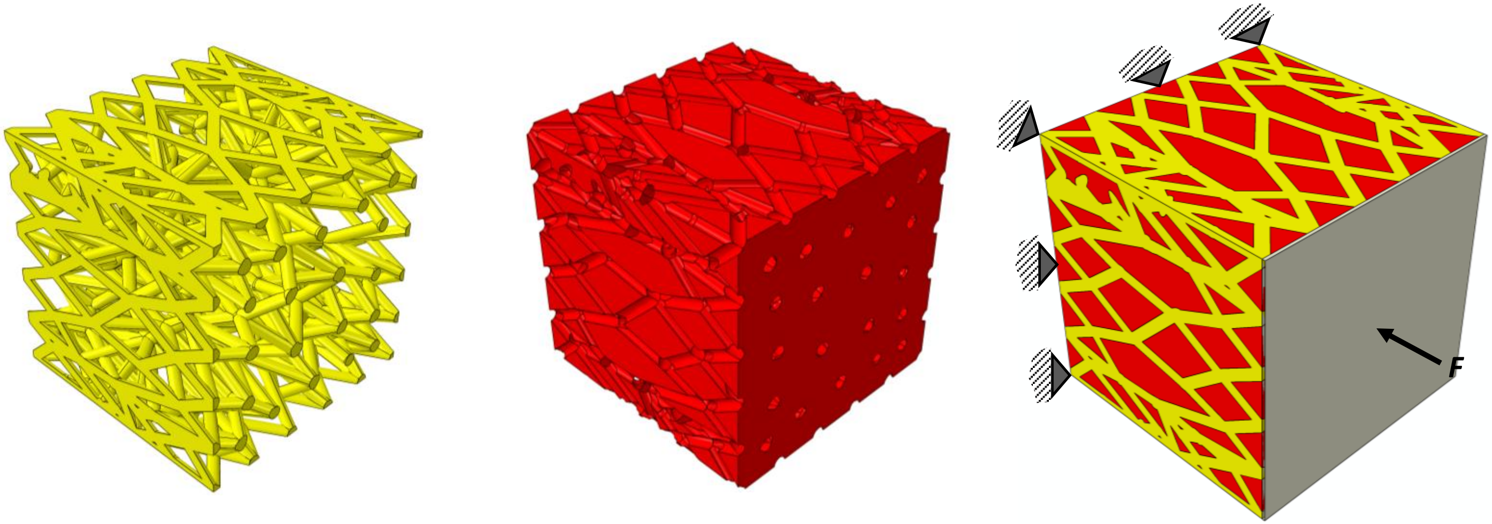
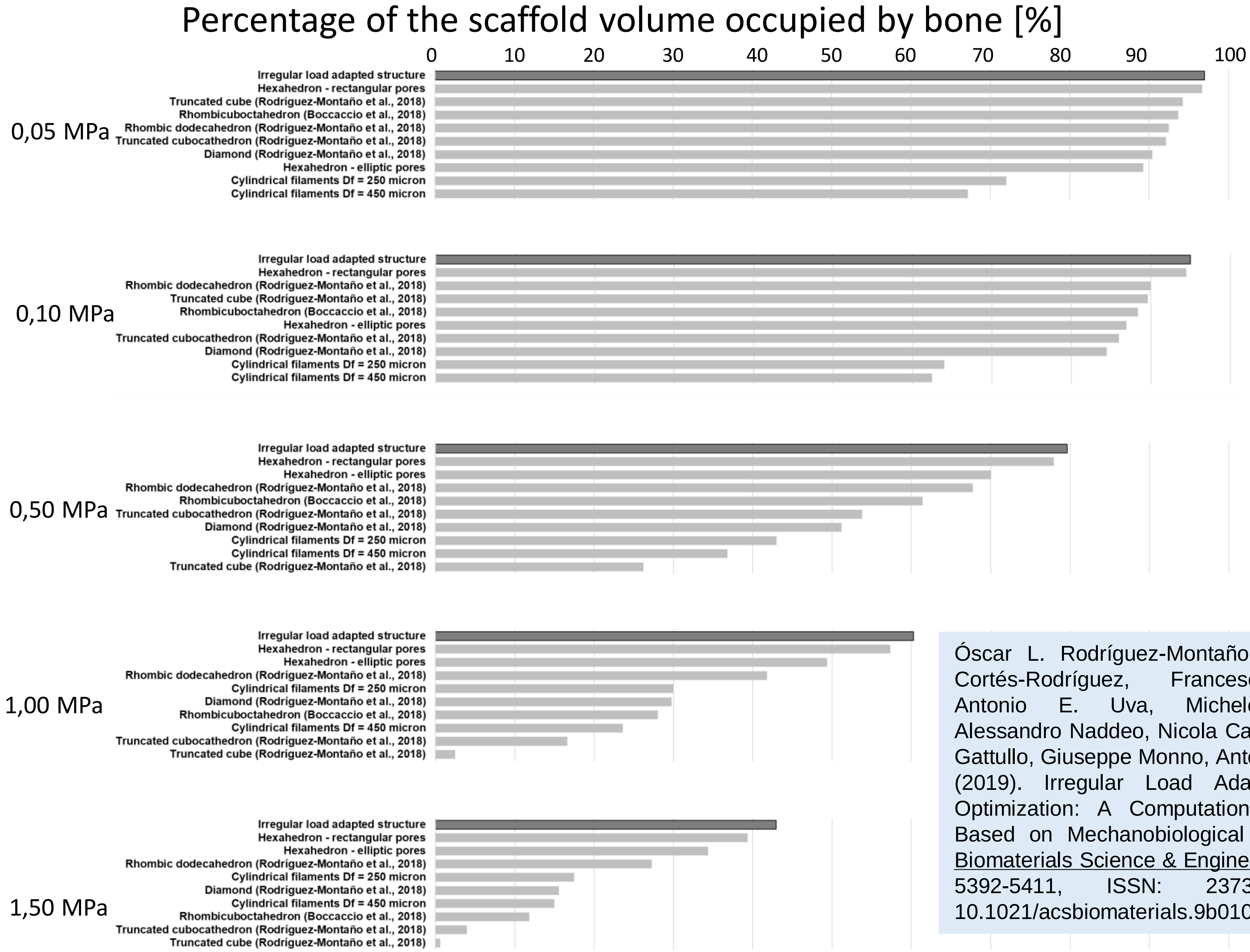


But…if irregular load adapted scaffolds are considered…



Comparison


Percentage of the scaffold volume occupied by bone [%]

Óscar L. Rodríguez-Montaño, Carlos Julio Cortés-Rodríguez, Francesco Naddeo, Antonio E. Uva, Michele Fiorentino, Alessandro Naddeo, Nicola Cappetti, Michele Gattullo, Giuseppe Monno, Antonio Boccaccio (2019). Irregular Load Adapted Scaffold Optimization: A Computational Framework Based on Mechanobiological Criteria. ACS Biomaterials Science & Engineering, vol. 5, p. 5392-5411, ISSN: 2373-9878, doi: 10.1021/acsbiomaterials.9b01023

Limitations

- ☐ The optimal dimensions are based on the stimulus distribution predicted at the instant immediatly after the scaffold implantation.
- ☐ Angiogenesis and growth factors, were not included in the model.
- ☐ Any scaffold dissolution processes have also been neglected.

Perier-Metz C, Duda GN, Checa S. Initial mechanical conditions within an optimized bone scaffold do not ensure bone regeneration - an in silico analysis. Biomech Model Mechanobiol. 2021 Oct;20(5):1723-1731. doi: 10.1007/s10237-021-01472-2.

Conclusions

- A mechanobiology-based algorithm was developed capable of predicting the best scaffold micro-structure, i.e. the optimal dimensions of the pores that allow the amounts of bone generated within the scaffold, to be maximized.
- "Oriented" pores allow greatest amounts of bone to be generated than the "not oriented" ones.
- For increasing values of load, decreasing dimensions of the scaffold pores are predicted.
- Among the regular scaffolds, those with hexahedral unit cell / rectangular pores are the most performing.
- However, for all the values of the hypothesized compression load, the best scaffold type appears to be the irregular load adapted scaffold.

Thank you
for your attention